SUPPORT FOR THE AMENDMENTS

Support for the amendment of the claims can be found in the original claims and in the specification at pages 56-77. Applicants have added new claims 18-27 consistent with the restriction requirement and election of a single disclosed species. Support for claim 28-31 is found in claims 16 and 17 as originally presented. No new matter would be added to this application by entry of this amendment. Upon entry of this amendment, claims 1-15 and 18-31 will now be active in this application.

REQUEST FOR RECONSIDERATION

The present invention is directed to compounds which are useful for inhibiting matrix metalloproteinasses or tumor necrosis factor a, to pharmaceutical compositions comprising these compounds and salts, and to methods of using and producing these compounds and salts.

The rejection of Claims 15-17 under 35 U.S.C. 112, first paragraph, is respectfully traversed.

The present invention is described in such a manner as to enable one skilled in the art to which it pertains to make and use the claimed invention, without undue experimentation.

The use of the inhibitors of matrix metalloproteinases and tumor necrosis factor α to treat and prevent many disease processes is known. It is well-known in the art, and cited in the specification, that matrix metalloproteinases and tumor necrosis factor a play critical roles in many physiological mechanisms, as well as in diseases such as arthritis, cancer, cardiovascular disease, tissue ulceration, and fibrosis. Specification, page 74. Research has shown, and one skilled in the art would know, that the use of various inhibitors of MMP and TNF-α is effective in treating and preventing many of these diseases in animal models, and

that these treatment modalities show great promise in human medicine. The preparation of the active ingredients in the MMP and TNF-α inhibitors is described. The specification in the instant application discloses in great detail the process for preparing the object compounds. Specification, pages 56-73. The specification in the instant application further illustrates the *in vitro* efficacy of the described compounds in inhibition of MMP-1, MMP-9, MMP-13, and MMP-8. Specification, pages 74-77. One skilled in the art would recognize that this *in vitro* efficacy indicates promise for use *in vivo* for treatment of MMP-mediated diseases. One skilled in the art would know how to conventionally transform the object compounds into pharmaceuticals. The specification points out that these compounds can be isolated, purified, and transformed into their salts in a conventional manner. Specification, page 73-74. The specification describes the use of the object compounds as the active ingredient in an admixture with various carriers and other complementary substances and excipients. Specification, page 76. It also describes the use of the object compound as a pharmaceutical in various dosage forms, and describes the usage of varying dosages of the active compound. Specification, page 76. One skilled in the art would know how to combine the object compound with the other compounds, and one skilled in the art would expect there to be variations in dosages and methods of administration in order to affect an appropriate response. Indeed, any experimentation required to determine the most effective route and dosage of compound would not be undue, given the various disease processes involved and the differences among patients. Finally, one skilled in the art would know how to administer the pharmaceutical made from the object compounds.

Because one skilled in the art would be able to practice the invention claimed without undue experimentation, withdrawal of the enablement rejection is respectfully requested.

Moreover, the description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *See In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971). The examiner must have a reasonable basis to challenge the adequacy of the written description, and has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in the disclosure a description of the invention defined by the claims. *See* MPEP § 2163. In the instant application, the examiner has not met the burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in the disclosure a description of the invention defined by the claims. For that reason, Applicants respectfully request the reconsideration and withdrawal of this rejection.

The rejections of Claims 13-15 and 17 were rejected under 35 U.S.C. 101 and under 35 U.S.C. 112, second paragraph have been obviated by appropriate amendment.

Claims 13-15 have been amended to recite an active step. Claim 17 has been cancelled. Applicants respectfully request their allowance in their present form.

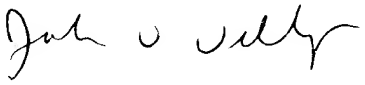
The rejection of Claims 15-17 were rejected under 35 U.S.C. 112, second paragraph has been obviated by appropriate amendment.

Claim 15 has been amended, and Claims 16-17 have been cancelled. Applicants respectfully request allowance of Claim 15 in its present form.

Applicants submit that this application is now in condition for allowance and early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



Norman F. Oblon
Attorney of Record
Registration No. 24,618

Richard L. Chinn, Ph.D.
Registration No. 34,305

John Dellinger
Registration No. 50,436
Registration No. 38,779

22850

(703) 413-3000
Fax #: (703)413-2220
NFO:RLC:JDD/cja

MARKED-UP COPY OF CLAIMS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN THE CLAIMS

13. (Amended) [Use] A method for treating, reducing, arresting, or alleviating matrix metalloproteinases (MMP) or tumor necrosis factor α (TNF α)-mediated disease, the method comprising administering to a patient a therapeutically effective amount of the compound of Claim 1 or a pharmaceutically acceptable salt thereof [as a medicament].

14. (Amended) [Use] A method for inhibiting matrix metalloproteinases (MMP) or tumor necrosis factor α (TNF α), the method comprising administering to a patient an effective amount of the compound of Claim 1 or a pharmaceutically acceptable salt thereof [as an inhibitor of matrix metalloproteinases (MMP) or tumor necrosis factor α (TNF α)].

15. (Amended) A process for manufacturing a medicament, said process comprising contacting [Use of] the compound of Claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable carrier [for manufacturing a medicament for treating for treating and/or preventing MMP- or TNF α- mediated diseases].

Claim 16-17 (Cancelled)

Claims 18-31 (New)

I:\atty\Jdd\210100US-amendment(revised).wpd